

**REMARKS**

The specification is amended to delete inadvertent reference to claims and to add priority information. Claims 1, 4, 5, 7, 11, 13, 14 (withdrawn), 16, 19 26 and 30 have been amended. These amendment include incorporation of the language of claims 2, 3, 6 and 12 into claim 1, with cancellation of these dependent claims.

It is submitted that no new matter has been introduced by the present amendments and entry of the same is respectfully requested.

**Claims 23-25, 32-38 were earlier withdrawn** from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions. As noted in the Office Action, Applicants elected the following “species”:

1. Protein binding domains (PBDs) of synaptotagmin SytI as species of PBDs;
2. synaptotagmin SytIV as target epitope;
3. gene 10B encoding the 10B capsid protein as the gene encoding the capsid protein;
4. 1 as a value for the integer *n*;
5. between 100 and 200 base pairs as the length of the cDNA molecules,

As for these elected species, the only capsid protein remaining in the claims in addition to the elected species, 10B, the protein 10A.

Claims 13, 15, 17 and 18, which were withdrawn as being directed to unelected species, are included in the Listing of Claims, as these claims are rejoivable, although they have not yet been formally examined. Claim 13 has been amended to change its dependency, reflecting cancellation of its base claim, claim 12.

Claim 20-22 seem to have been treated as a genus, so that the above election #5 corresponds to the language of claim 22. Nevertheless, all four of these claims were formally examined, and none were explicitly said to be withdrawn by the Examiner. Applicants request a clarification of the status of these claims.

The “part” of claim 30 which is believed to have been excluded from the Examination because, as Applicants understand, it was deemed to be withdrawn as nonelected species, is denoted as section (b) of the claim. This section has been retained for consideration of rejoinder.

Claims 1-12, 14, 16, 19-22, 26 and 30 (in-part) were examined. Applicants respectfully submit that the claims are now in condition for allowance.

## **I. OBJECTIONS TO THE SPECIFICATION AND INFORMALITIES**

### **A. Priority**

The specification has been amended at page 1 to insert a reference to the provisional application from which this application claims priority.

### **B. Other informalities**

The disclosure was objected to because the specification at page 12, line 19, referred to “claims 5 and 6” which is improper. The Office required appropriate correction. The specification has been amended to remove the improper references to claims.

The Office objected to the use of trademarks at several locations without the requisite capitalization and trademark symbols. Applicants wish to defer for now and will amend all such references once patentable subject matter has been indicated by the Office.

## **II. REJECTIONS UNDER § 112, SECOND PARAGRAPH**

Claims 1-12, 14, 16, 19-22, 26 and 30 (in-part) were rejected as being indefinite for a number of reasons set forth below.

### **A. Lack of Antecedent Basis for T7 Phages**

Claim 1 recites the limitation “said T7 phages” in step (a) lines 2-3, but there is insufficient antecedent basis for this limitation. The word “said” has been deleted.

### **B. “Bindable Array”**

Claim 1 recites “bindable array of target epitopes”, which the office finds unclear as to the term “bindable.” The Examiner asks whether Applicants mean that the array can be bound or does applicants mean that the array has charged groups or epitopes of the array that are specific to the potential binding domains of the phage display library. Applicants were requested to clarify.

The term “bindable” has been deleted. It is believed that the language of claim 1(b) complies with § 112, 2<sup>nd</sup> paragraph.

### **C. “Families” of Epitopes**

Claim 1 recites ‘families of epitopes’ which is not clear to the Office. The Examiner asks whether applicants mean that the epitopes and the related epitopes share the same structural features or functional features. The specification allegedly lacks a definition for the “family of epitopes.”

First, claim 1 has been amended to better define “family” of epitopes. The Examiner’s attention is directed to the definition of “family” in the specification, in the paragraph bridging pages 11-12, reproduced below (emphasis added):

The target epitopes indicated above are preferably peptide epitopes and the **family** preferably **comprises** peptides or polypeptides corresponding to (i) a protein fragment, (ii) a protein domain or (iii) a complete protein. The **family** preferably **comprises** a progressive series of overlapping peptides of about 10 to 15 amino acids, each of which peptides lacks **n** amino-terminal amino acid residues of its predecessor peptide in the series and has at least **n** additional amino acids added to its carboxy-terminus, wherein **n** is an integer between 1 and 5, , and wherein the series of overlapping peptides corresponds to (i) a region of the protein of up to about 100 amino acids, or (ii) the complete protein.

**D. Claim 1(e)**

The Office notes that Claim 1 in step (e) recites “...determining the DNA sequence encoding the PBDs...” and the last two lines of the claim recite “... thereby identifying the PBDs displayed on said eluted phage by their predicted amino acid sequence.” It is noted that the claimed method **does not recite “predicting the amino acid sequence”** and the Examiner inquires whether Applicants meant to recite further “by the predicted nucleic acid sequence”.

The language of claim 1(e) has been amended to overcome this objection.

**E. Lack of Antecedent Basis in Several Claims**

Claim 2 recites the limitation “the target epitope” in step (ii) but lacks a sufficient antecedent basis. This claim has been cancelled and its language incorporated into claim 1 in a way that cures this deficiency.

Claim 6 recites the limitation “said outer surface protein capsid protein”. There is insufficient antecedent basis for this limitation in the claim or in claim 1. This claim has been cancelled and its language incorporated into claim 1 in a way that cures this deficiency.

Claim 14 recites the limitation “said target peptides”. There is insufficient antecedent basis for this limitation in the claim or in claim 1. The amendment of claim 1 corrects this deficiency.

It is believed that the present amendments have mooted all the foregoing grounds for rejection, which may properly be withdrawn.

### **III. REJECTIONS UNDER § 112, FIRST PARAGRAPH -- WRITTEN DESCRIPTION**

The Office rejected all pending claims under 35 U.S.C. § 112, first paragraph, as lacking adequate written description.

#### **A. The Standard**

The standard for a rejection based on inadequate written description was set out by the Federal Circuit in *Vas-Cath Inc. v. Mahurkar*, 19 USPQ2d 1111, 1116 (Fed. Cir. 1991) (quoting *In re Smith*, 178 USPQ 620, 623-624 (CCPA 1973)):

In order to determine whether a prior application meets the “written description” requirement with respect to later-filed claims, the prior application need not describe the claimed subject matter in exactly the same terms as used in the claims; it must simply indicate to persons skilled in the art that as of the earlier date the applicant had invented what is now claimed.

See, also, *In re Wertheim*, 191 USPQ 90, 98 (CCPA 1976) (“Lack of literal support . . . is not enough . . . to support a rejection under §112.”). The *Wertheim* court further pointed out, *supra* at 96, that

The function of the description requirement is to ensure that the inventor had possession, as of the filing date of the application relied on, of the specific subject matter later claimed by him; how the specification accomplishes this is not material. (*In re Smith*, 178 USPQ 620)... It is not necessary that the application describe the claim limitations exactly, *In re Lukach*, 169 USPQ 795 (1971), but only so clearly that persons of ordinary skill in the art will recognize from the disclosure that appellants invented processes including those limitations. *In re Smythe*... 178 USPQ 279,284 (CCPA 1973).

#### **B. The Rejection and Applicants Response**

Applicants are somewhat confused by the formulation of the Office’s grounds for rejection but will do their best to discuss and set forth their disagreement where appropriate. The claims were rejected as failing to comply with the **written description** requirement – that the claimed subject matter was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors, at the time the application was filed, had possession of the claimed invention. Below, various aspects of the rejection are discussed, and Applicants’ comments and statements of their position are interspersed (in a different font).

The instant claims recite, in brief, a screening method for identifying in a library of potential binding domains (PBDs), a polypeptide binding domain that bind to a target epitope comprising,

- (a) providing a cDNA library that encodes a library of PBDs as a T7 phage display library;
- (b) contacting the phage display library with an array of target epitopes or families of epitopes under conditions where any of said PBDs binds to its target epitope[s]
- (c) removing unbound T7 phage from the array of target epitopes;
- (d) eluting bound T7 phage;
- (e) determining the DNA sequence encoding the PBD and thereby identifying the PBDs.

According to the Office Action, the specification discloses in general peptide display technology and methods of using T7 phage in screening, and methods of screening double unknowns using known phage display versus known multipin technology. Further the specification teaches methods for identifying the interactions between Synaptotagmin I and Synaptotagmin IV. The specification discloses methods for testing the known (*which applicants read as meaning “predetermined”*) PBDs and target epitopes (*i.e.*, see pages 40-41). While the Office agrees that the specification discloses the use of phage display technology and Multipin in screening or identifying protein interactions, the Office’s asserts that the specification does not disclose adequately the “**use of the claimed method in identifying potential binding domains.**” Allegedly, this is because the **Examples** are drawn to Synaptotagmin (Syt) interactions, and Synaptotagmin-Syntaxin interactions, which are allegedly “**different from the claimed method of identifying potential binding domains.**”

*Again, applicants interpret “different” to mean that the originally claimed methods relied on the use of “unknown” or “not predetermined” PBDs.*

The Office further asserts that Applicants’ disclosure is drawn to a specific T7 vector with 10B capsid protein of T7. The Office concluded that the **description “clearly do not provide adequate representation regarding the open ended method of instant claim.”**

*Applicants interpret this to mean that, in the Office’s view, the specification lacks adequate written description for claims that read on T7 vectors in which any T7 capsid protein other than 10B is utilized. Applicants point out that, as discussed at length in the specification (page 18, line 13- page 22, the T7 vector system is well-known in the art, and commercially available. Capsid proteins 10A and 10B are modified versions of the same gene product provided by the vendor as choices. Thus, despite the fact that an embodiment with capsid protein 10B is exemplified, there is no basis in fact for a conclusion that a person of skill in the art familiar with this well-known vector system, and*

*reading the specification would conclude that the only invention that Applicants' possess is one in which the 10B capsid protein, but not the 10A protein, is employed. Applicants believe that is totally evident that the inventors intended and has in "their possession" embodiments that employed 10A, as was explicitly disclosed in the specification.*

Case Law Cited by the Office

The Action directs Applicants' attention to the Federal Circuit's decision in *University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398 (1997), for its holding that "written description ... involving a chemical genus, like a description a chemical species, 'requires precise definition, such as structure or formula or chemical name' of the claimed subject matter sufficient to distinguish it from other materials." (at page 1405, quoting *Fiers v. Revel*, 25 USPQ2d 1601 (Fed. Cir. 1993).

The Action asserts that this holding is applicable to the present claims which allegedly also lack a "showing of sufficient identifying characteristics" or "examples of claimed method or the potential binding domains identified by the claimed method," as would be required to demonstrate "possession of claimed generic."

The Action further asserts that the disclosure is "**hypothetical**" and based on identifying protein-protein interactions and is **not drawn to identifying potential binding domains as claimed**. The Office asserts that the **description is "based on known proteins and the interactions between the proteins using two well ???? (apparently "known" was intended) combinatorial and recombinant technologies**" whereas the specification has **not disclosed the claimed method of identifying the potential binding domains**. The specification allegedly **does not exemplify PBDs identified using the claimed method**. Thus the specification lacks written description.

*Again, Applicants do not understand the precise meaning of the foregoing points made by the Office, unless this is just another way of stating the same points that were stated earlier in the Action.*

*If Applicants' understanding is correct, then the primary bases of this § 112, first paragraph rejection would be overcome if two issues were addressed.:*

- (1) *claim 1 was limited to the scope of claim 2 or 3, wherein one class of binding partners of the two involved (i.e., PBDs or target epitopes) were predetermined ("known"), as in claim 2. Claim 3 further limits claim 2, and thereby claim 1, in that it requires specifically that the target epitope or family of epitopes be predetermined.*

*Applicants have introduced the language of claim 3 into claim 1, and believe that this amendment removes this ground for rejection. Furthermore, this “family” of epitopes is defined more clearly by the introduction of the language of claim 12 into claim 1.*

- (b) *the T7 phage outer capsid protein which is made into a fusion protein in the present method were limited to the 10B protein.*

*As applicants noted above, there is no reason why a claim limited to “10A or 10B” would not be adequately described by the specification, particularly in light of the knowledge in the art, the fact that these are commercially available products being incorporated into applicants’ new methods. Thus, the language of claim 6 has been incorporated into claim 1, so that the claim is now limited to using T7 10A or 10B capsid proteins. Dependent claim 7, and additional claims dependent thereon, further limit the method to the use of capsid protein 10B.*

#### **IV. REJECTIONS UNDER 35 U.S.C. § 102**

The Examiner’s Action rejected various claims 1-5, and 8-12 under 35 U.S.C. § 102(b) as being anticipated by Houshmand et al (*Analytical Biochemistry* 268 363-370, March 1999) for the reasons detailed below. In light of the foregoing amendments to the claims and the following discussion, it would be appropriate to withdraw these grounds of rejection.

##### **A. Legal Test for Novelty:**

“Anticipation requires the presence in a single prior art disclosure of all elements of a claimed invention arranged as in the claims”. *Jamesbury Corp v. Litton Industrial Products, Inc.*, 225 USPQ 253, 256 (Fed Cir 1985). It is axiomatic that for prior art to anticipate under § 102 it has to meet every element of the claimed invention...” *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 231 U.S.P.Q. 81, 90 (Fed. Cir. 1986). Moreover, the cited reference must enabling, as the Federal Circuit stated in *In re Donohue*, 226 USPQ 619, 621 (Fed. Cir. 1985): “even if the claimed invention is disclosed in a printed publication, that disclosure will not suffice as prior art if it was not enabling.”

B. Rejection under § 102(b) and Discussion:

1. Claims 1-5 and 8-12 were rejected as being anticipated by Houshmand *et al.*,

*Analytical Biochemistry* 268 363-370, March 1999 (“Houshmand”).

“Houshmand” allegedly discloses a heptapeptide library displayed by bacteriophage T7 (referring to the abstract of this paper) which the Office equates with step (a) of instant claim 1. As characterized by the Office, “epitopes of monoclonal antibodies F4, F5 and LT1 were adsorbed to the wells of microtiter plate. This was equated to “the array of epitopes” of instant claim 1. Viruses (the phage library) were adsorbed to the mAb-coated wells. This is equated to step (b) of instant claim 1. Phage particles adsorbed to the coated surface were eluted by SDS, and the eluted phage were amplified in *E. coli* (*i.e.*, right column in page 4, under “panning procedure”). This was equated with claim 1 (d) and (e) and claim 11. The selection was repeated four times, equated to instant claim 4. After final panning the phage was cloned by plaque isolation. For analysis of expressed peptide sequences, a segment of the phage DNA was amplified by PCR the nucleotide sequences of the DNA products were then determined (equated to claim 1(e)) of the instant claims). The reference discloses the fusion polypeptide present in 415 copies on each phage particles. This is equated to claims 8 and 9.

Applicants’ Response

Claims 6 and 7 are said to be free of this rejection. For this reason, Applicants believe that claims 8-12 should also be considered free of this rejection because claim 8-10 depend from claim 7, which is admittedly not anticipated.

Since the language of claim 6 has been incorporated into claim 1, then all the claims previously rejected over this reference are, by definition, free of this reference. Houshmand as a prior art reference would fail to meet the legal requirements for anticipation of amended claim 1.

Applicants note further that the Office Action failed to appreciate another distinction between this reference in claim 1, according to which Houshmand would not meet the *prima facie* requirements for anticipation. Houshmand uses a random hexapeptide T7 library. In contrast, claim 1(a) involves “predetermination” of the members of the T7 library since it is made from cDNA from a biological source of interest for which binding partners are being screened.

... (a) providing a cDNA library from said source that encodes said library of PBDs as a T7 phage display library

This is clearly not the case in Houshmand. This point is also germane to the obviousness rejections in which Houshmand is the primary reference. Thus, as for anticipation, even in the absence of the amendments to claim 1, it and dependent claims thereon that had been rejected under §102 (b) should still be considered novel over Houshmand. In view of the foregoing, it would be proper to withdraw this ground for rejection.

## V. REJECTIONS UNDER 35 U.S.C. § 103

The Office Action sets forth two grounds for rejecting the claims as obvious under §103(a). For the reasons detailed below, Applicants respectfully submit that in light of the foregoing amendments, it would be appropriate to withdraw these grounds of rejection.

### A. Legal Test for Nonobviousness:

The burden of establishing a case of *prima facie* obviousness rests with the Office. *In re Fine*, 5 USPQ2d 1596, 1598 (Fed. Cir. 1988). Moreover, an obviousness rejection “must be based on evidence (statutory prior art, admissions against interest)... .” *In re McKellin*, 188 USPQ 428, 432 (CCPA 1976), emphasis in original. The Federal Circuit has repeatedly articulated the requirements of a proper analysis:

[W]here claimed subject matter has been rejected as obvious in view of a combination of prior art references, a proper analysis under § 103 requires, *inter alia*, consideration of two factors: (1) whether the prior art would have suggested to those of ordinary skill in the art that they should make the claimed composition or device, or carry out the claimed process; and (2) whether the prior art would also have revealed that in so making or carrying out, those of ordinary skill would have a reasonable expectation of success. *See In re Dow Chemical Co.*, ... 5 USPQ2d 1529, 1531 (Fed. Cir. 1988). Both the suggestion and the reasonable expectation of success must be founded in the prior art, not in the applicant’s disclosure.

*In re Vaeck*, 20 USPQ2d 1438, 1442 (Fed. Cir. 1991).

It respectfully is submitted that a legally sufficient *prima facie* case of obviousness has not been adduced because the cited art does not suggest that the methods claimed be carried out. The Office Action does not appear to focus on the claimed invention taken as a whole. The hindsight assembling of the references cited against an applicant’s claims, as has been done here, is legally improper according to the case law, such as *Orthopedic Equipment Co.* cited above. This “is a legally improper way to simplify the often difficult determination of obviousness.” *The Gillette Co. v. S.C. Johnson & Sons, Inc.*, 16 USPQ2d 1923, 1927 (Fed Cir. 1990), citing with approval, *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 231 USPQ 81 (Fed. Cir. 1986), *cert. denied*, 480 U.S. 947 (1987). In other words,

It is wrong to use the patent in suit as a guide through the maze of prior art references, combining the right references in the right way so as to achieve the result of the claims in suit.

*Orthopedic Equipment Company v. U.S.*, 217 USPQ 193, 199 (Fed. Cir. 1983). The nonobviousness of the claimed invention is discussed in detail below.

B.. Specific Rejections and Discussion:

1. First Obviousness Rejection:

Claims 1-12 and 20-22 were rejected as being obvious over Houshmand (*supra*) and Studier *et al.*, US Patent 5,766,905 (“Studier”). The disclosure of Houshmand and its “matching” to certain claims, as alleged by the Office, are discussed above.

The Office admits that the claimed invention differs from Houshmand due to the inclusion in the claims (originally in claims 6-10; now in claim 1) of the limitation requiring the outer surface protein of T7 phage to be either 10A or 10B, which is not taught by Houshmand.

Studier allegedly fills that gap. Studier describes a cytoplasmic phage display system based on T7 wherein the display vectors comprise DNA encoding a portion of structural protein from a “cytoplasmic bacteriophage” joined covalently to a protein or peptide of interest. The reference discloses fusion in which protein or peptide sequence of interest is fused at amino acid 348 of the T7 10B capsid protein. The reference is said to teach

- (1) “that the display vectors of the present invention<sup>2</sup> can be used ... to screen or select virus bearing capsid fusion proteins,” and
- (2) “expression screening of DNA library in an effort to identify a protein having particular binding characteristics.”

On this basis, the Office concluded that, it would have been [*apparently the term “obvious” was omitted here*] to use the T7 capsid protein 10B to fuse with a peptide of interest in a method of screening a DNA library for identifying a protein or peptide having particular binding characteristics. The Office asserts that a person skilled in the art would have been **motivated to use the 10B capsid protein** to fuse the peptide of interest such that the fusion protein is displayed because Studier allegedly teaches advantages of using C-terminus of the T7 10B capsid protein.

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<sup>2</sup> Applicants are not sure whether by “present invention” the Office Action refers to the claims being examined or the invention disclosed in Studier. It is assumed that the Office means the Studier invention, as it is presumably the uses of the Studier display vectors that is serving as prior art against the present claims.

### Applicants' Response

As noted in the discussion above of the §102 (b) rejection, Houshmand does not meet the criteria required of a primary reference in supporting a *prima facie* obviousness rejection, since it does not adequately disclose all that the Office is asserting. There is no basis in Houshmand for using a preselected or predetermined cDNA library as a T7 phage display library as required in original claim 1; this deficit holds true *a fortiori* after the present amendments to claim 1. Therefore, given the inadequacy of Houshmand, this obvious rejection should fail *a priori* or be withdrawn in light of the amendments to claim 1. Studier does not fill the gap left by Houshmand with respect to use of a non-random peptide library, such as predetermined library in the form of a cDNA library from a biological source that is recited in claim 1.

Despite, the alleged obviousness, the Office has not cited any reference, and the Applicants know of none at the time the invention was made, that specifically describe the use of a cDNA library as a phage display library in the T7 system. Applicants do not challenge the fact that their use of T7 phage display employing the 10B capsid protein, was known in the art (e.g., the cited Studier reference). However, prior to their invention, no reference disclosed or even suggested combining this approach with other recited steps to reach the presently claimed invention. There was no suggestion in the art to:

- (A) make a Studier-type of T7 phage display library of potential binding domains from a cDNA library which represent the expressed proteins of a ***predetermined*** source of cells **AND**
- (B) contact this library with an array of peptide epitopes (*i.e.*, the “bait”), selecting thus display library members to bind to their target epitopes **AND**
- (C) isolate bound phage, sequence their DNA to find out what binding domains were encoded in that cDNA library of predetermined origin.

It is important to keep in mind the conceptual difference between starting with a cDNA library vs. a random peptide library. In the latter, each phage that is expected to bind to the bait protein or peptide must contain a consensus sequence that represents all or most of a binding region. After going through the step of sequencing the bound phage, one expects to find a commonality among all those phages bound. Only with such an outcome is the screen a success. In contrast, using the present method, one expects to screen and find all phages that display an amino acid sequence that binds to any one of several possible binding partners represented in the preselected peptide binding

epitope “family” represented in the array of claim 1(b). One is not searching for a single consensus sequence. The present method reveals phages that display a broader range of interacting peptides that are mappable to one or more interacting protein domains present in the cells that were the source of the cDNA.<sup>3</sup>

In view of the amendments and foregoing remarks, Applicants believe it would be proper to withdraw this ground of rejection.

## 2. Second Obviousness Rejection

Claims 1-12, 14, 16, 20-22 were rejected as being obvious over Houshmand (*supra*), Studier (*supra*) and Geysen (US Patent 4,833,092). The reasons for citing Houshmand and Studier were discussed above.

According to the Office, the invention (presumably that defined by claims 14 and 16) differs from Houshmand and Studier in the recitation of target epitopes (target peptides) synthesized in parallel on polyethylene pins. Houshmand and Studier are said to teach different methods of preparing phage display libraries and methods of screening the library using multiple targets arranged in arrays, but do not teach target epitopes arranged or synthesized on polyethylene pins. The Office asserts that it is well known in combinatorial solid phase synthesis technology to use “Multipins” in arrays compatible with standard 96 well microplates. Geysen allegedly teaches synthesis of peptides on polyethylene pins. The present specification (page 8 last paragraph through page 9) discloses that

...simultaneous synthesis of numerous individual peptides of known sequence on a solid support array, such as on “Multipins” that are arrayed in a manner complementary to the wells of standard 96-well microplates. This is preferably done using the MULTIPIN peptide synthesis kit from Chiron or by similar methods such as those described in US Patent 5,266,684, 5,266,684, 5,010,175, 5,182,366, 5,194,392 and 4,833,092...

The Office Action concludes that it would have been obvious to use the well-known, and commercially available, Multipin technology to synthesize target peptides on Multipins that fit the 96 well microtiter plate format, wherein the wells contain a phage display library. It appears that this rejection is directed specifically to claims 14-16 (and, likewise, to withdrawn claims 15, 17 and 18).

As above, Applicants do not challenge the fact that their use of T7 phage display, employing the 10B capsid protein was known in the art, nor do they challenge the fact that use of the Geysen Multipin technology was known in the art. However, they reiterate their remarks made above in

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<sup>3</sup> using additional steps of this invention that are recited in withdrawn claims (e.g., claims 23-25 and 32-37). Directed to

discussing the first § 103 rejection. Geysen does not fill the gaps left by Houshmand as the primary reference even when combined with Studier as a secondary reference. The fact that Applicants' method employs a known method (that of Geysen) to synthesize and display the target peptides on Multipin arrays, does not detract from the unobviousness of the combination of steps, starting from a cDNA library from a preselected source of cells ("biological source") rather than a random peptide library.

In view of the amendments and foregoing remarks, Applicants believe it would be proper to withdraw this second ground of rejection under § 103..

#### **VI. Indication of Allowable Subject Matter:**

The Office Action indicated that the claimed method for identifying a polypeptide binding domain using PBDs of SytI and SytIV (claim 30(a)) were free of the prior art and presumably allowable even in view of the rejection of certain claims for lack of written description. The Office failed to mention that claim 26 should be considered equally free of the cited art (although it was listed under the §112, first paragraph rejection). Applicants believe that the Office has not made a *prima facie* case for the rejection of claim 26 under §112, first paragraph. Particularly in view of the amendments to claim 1, claim 26 should fall in the same allowable category that the Office deemed appropriate for claim 30. Moreover, Appilicants request the Office to now examine the unelected species (and claims 13, 15, 17, 18 and 30b) for rejoinder with the claims directed to the elected species.

#### **VII. Conclusions**

In conclusion, it is respectfully requested that the above amendments, remarks and requests be considered and entered. Applicant respectfully submits that all the present claims, as amended, meet the requirements of 35 U.S.C. §112, first and second paragraphs, are free of the previous art rejections, and are in condition for allowance. Applicants respectfully request early notice of such favorable action.

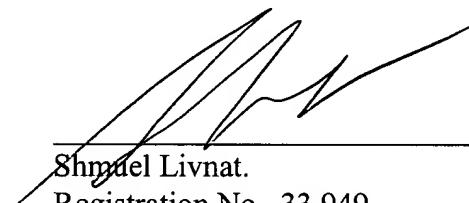
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other embodiments.

**Examiner Ponnaluri is respectfully requested to contact the undersigned at (202) 334-8584 with any questions or comments if they will assist in the understanding this amendment and response. The undersigned requests the opportunity for a personal interview before the Examiner next acts on this case.**

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 22-0261**.

Respectfully submitted,



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